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The low global burden of trichinellosis: evidence and implications

Devleesschauwer, Brecht ; Praet, Nicolas ; Speybroeck, Niko ; Torgerson, Paul R ; Haagsma, Juanita A
; De Smet, Kris ; Murrell, K Darwin ; Pozio, Edoardo ; Dorny, Pierre

Abstract: Trichinellosis is a cosmopolitan foodborne disease that may result in severe health disorders and even death. Despite international awareness of the public health risk associated with trichinellosis, current data on its public health impact are still lacking. Therefore we assessed, for the first known time, the global burden of trichinellosis using the Disability-Adjusted Life Year metric. The global number of Disability- Adjusted Life Years due to trichinellosis was estimated to be 76 per billion persons per year (95% credible interval: 38–129). The World Health Organization European Region was the main contributor to this global burden, followed by the WHO region of the Americas and the World Health Organization Western Pacific region. The global burden of trichinellosis is much lower than that of other foodborne parasitic diseases and is in sharp contrast to the high budget allocated to prevent the disease in many industrialised countries. To decrease the uncertainty around the current estimates, more knowledge is needed on the level of underreporting of clinical trichinellosis in different parts of the world.

DOI: <https://doi.org/10.1016/j.ijpara.2014.05.006>

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ZORA URL: <https://doi.org/10.5167/uzh-108995>

Journal Article

Accepted Version

Originally published at:

Devleesschauwer, Brecht; Praet, Nicolas; Speybroeck, Niko; Torgerson, Paul R; Haagsma, Juanita A; De Smet, Kris; Murrell, K Darwin; Pozio, Edoardo; Dorny, Pierre (2015). The low global burden of trichinellosis: evidence and implications. *International Journal for Parasitology*, 45(2-3):95-99.

DOI: <https://doi.org/10.1016/j.ijpara.2014.05.006>

International Journal for Parasitology

Succinctus

The global burden of trichinellosis

Brecht Devleesschauwer^{a,b,*°,}, Nicolas Praet^{c,*}, Niko Speybroeck^b, Paul Torgerson^d, Juanita A
Haagsma^e, Darwin Murrell^f, Edoardo Pozio^g, Pierre Dorny^{a,c}

^a *Department of Virology, Parasitology and Immunology, Ghent University, Salisburylaan 133, 9820 Merelbeke, Belgium;*

^b *Institute of Health and Society (IRSS), Université catholique de Louvain, Clos Chapelle-aux-Champs 30, 1200 Brussels, Belgium;*

^c *Department of Biomedical Sciences, Institute of Tropical Medicine, Nationalestraat 155, 2000 Antwerp, Belgium;*

^d *Section of Epidemiology, Vetsuisse Faculty, University of Zürich, Winterthurerstrasse 270, 8057 Zürich, Switzerland;*

^e *Erasmus MC, Department of Public Health, P.O. Box 2040, 3000 CA Rotterdam, The Netherlands;*

^f *Department of Veterinary Disease Biology, Faculty of Health and Medical Sciences, University of Copenhagen, Stigbojlen 4, DK-1870 Frederiksberg C, Denmark;*

^g *Department of Infectious, Parasitic, and Immunomediated Diseases, Istituto Superiore di Sanità, viale Regina Elena 299, 00161 Rome, Italy.*

* These authors contributed equally to this work

° Corresponding author: Brecht Devleesschauwer; Department of Virology, Parasitology and Immunology, Ghent University, Salisburylaan 133, 9820 Merelbeke, Belgium; Tel.: +32 9 264 7328; E-mail: Brecht.Devleesschauwer@UGent.be

Highlights

- The global burden of human trichinellosis is low, with a mean estimated loss of 76 healthy life years per billion people per year.
- The WHO European region is responsible for 69% of the global burden.
- Chronic trichinellosis could significantly increase the global burden of trichinellosis, but there is large uncertainty about its true extent and nature.
- These findings support the revision of current *Trichinella* meat inspection regulations and their replacement by more cost-effective prevention programs.

Abstract

Trichinellosis is a cosmopolitan foodborne disease that may result in severe health disorders and even death. Despite international awareness on the public health risk associated with trichinellosis, data on its public health impact are still lacking. Therefore, we assessed for the first time the global burden of trichinellosis using the Disability-Adjusted Life Year (DALY) metric. The number of DALYs due to trichinellosis was estimated to be 76 per billion per year (95% CrI: 38–129), much lower than for other foodborne parasitic diseases and in sharp contrast to the high budget allocated to prevent the disease in many industrialized countries. To decrease the uncertainty around the current estimates, more knowledge is needed on the nature and extent of chronic trichinellosis and on the level of underreporting of clinical trichinellosis in different parts of the world.

Keywords

Trichinellosis; Global burden of disease; Disability-adjusted life years

1. Introduction

Trichinellosis is a foodborne helminthic disease caused by one of several *Trichinella* species (Pozio and Zarlenga, 2013). Infection occurs when humans consume raw or undercooked meat of different animal origins, e.g. pork, horse or game, containing muscle larvae (Gottstein et al., 2009). Clinical signs of trichinellosis are various and not pathognomonic, making the diagnosis complicated, which leads to medical misclassification and underreporting. In the acute phase of the disease, infected individuals may present with gastrointestinal disorders such as diarrhoea, but also with myalgia, fever, headache and facial oedema (Pozio et al., 2003). Whether or not a chronic form of trichinellosis exists is still under debate. The few studies that included follow-up over a longer time span indicated that myalgia and fatigue can persist for four months and, in a substantial proportion of cases, for up to two years (Nemet et al., 2009).

Although the actual public health impact of human trichinellosis has not yet been quantified, many industrialized countries are implementing strict and costly programmes to prevent the disease at the farm and slaughterhouse level. Indeed, each year, more than 167 million pigs are tested in the EU for *Trichinella* spp. by the artificial digestion method under the Commission Regulation (EC) 2075/2005 (Alban et al., 2011). With a mean expense of €1,31 per tested pig tested, a gross estimate of the annual cost linked to pig testing in the EU amounts to €220 million (Kapel, 2005). Other sources report an annual cost of about US\$ 570 million in the EU for inspection for *Trichinella* and US\$ 1 billion due to swine and human trichinellosis in the United States, primarily for health regulatory activities to prevent infection (Murrell and Pozio, 2000).

The aim of the current study is to provide the first global burden of disease assessment for trichinellosis, based on the Disability-Adjusted Life Year (DALY) metric. This assessment is part of a larger exercise of the World Health Organization (WHO) to assess the global burden of all major foodborne diseases (Torgerson et al., 2014).

2. Materials and methods

2.1. Incidence and mortality

The estimation of the global incidence and mortality of trichinellosis presented here is based on the results of a recent systematic review on the worldwide epidemiology and clinical impact of human trichinellosis between 1986 and 2009 (Murrell and Pozio, 2011). Searches of six international databases yielded 494 reports, of which 261 were selected for data extraction after applying strict relevance and reliability criteria. From 1986 through 2009, there were 65,818 cases and 42 deaths reported from 41 countries. The apparent annual incidence and mortality of trichinellosis was calculated by dividing the average number of cases and deaths in this 24-year period by the 1997 mid-year population (WHO, 1998). As in Murrell and Pozio (2011), we stratified our incidence and mortality rates by WHO region.

Because of the important variability in the reporting of the disease, the apparent incidence and mortality rates were adjusted to account for underreporting of the cases due to under-ascertainment, medical misclassification and/or absence of effective surveillance systems. Recently, Vu Thi et al. (2013) have shown that in a trichinellosis outbreak in Vietnam, 6 patients had sought health care while another 30 putative trichinellosis cases had not. As the detection of

putative trichinellosis cases was based on serology, the estimate of six "true" trichinellosis cases per "apparent" case is likely an overestimation. However, given the scarcity of data on the level of underreporting for trichinellosis, we applied this correction factor to the incidence and mortality rates in the AFRO, EMRO, SEARO and WPRO WHO regions, in order to obtain a plausible upper bound for the true incidence and mortality rates. For the EURO and AMRO WHO regions, where surveillance is likely more efficient, we arbitrarily applied, in the absence of any data, a correction factor of two, implying that for every reported case there is assumed to be a non-reported one.

2.2. Disability-Adjusted Life Years

The DALY metric has been developed as an alternative method to estimate, compare and rank the burden of diseases by including both fatal and non-fatal health outcomes. DALYs can be interpreted as the number of healthy life years lost due to a disease, and result from the sum of the number of years lived with a disability (YLDs) due to the disease, and the number of years of life lost due to disease-related mortality (YLLs) (Murray, 1994). This concept was first used in the Global Burden of Disease (GBD) study, a comprehensive assessment of the worldwide health impact of more than 100 diseases and risk factors. The calculations of the GBD have been updated several times by both the World Health Organization (WHO) and the Institute for Health Metrics and Evaluation (Murray and Lopez, 2013).

In an pathogen-based DALY calculation, DALYs are the sum of the YLDs for the non-fatal outcomes of the pathogen and the YLLs for the fatal outcomes (Mangen et al., 2013). The YLDs are calculated as the product of the number of cases, the duration of the outcome until remission

or death in years, and a disability weight (DW), expressing the severity of the outcome on a scale from zero to one. The YLLs are calculated as the product of the number of deaths and the standard life expectancy at age of death in years. Instead of absolute numbers, DALYs can also be calculated as rates, expressing e.g. the number of healthy life years lost per 100,000 people per year.

The incidence and mortality rates were estimated as described in section (2.1). To account for the uncertainty in the level of underreporting, we let the regional incidence and mortality rates vary uniformly between their raw and adjusted values. To be able to calculate sex and age stratified DALYs, we further stratified these incidence and mortality rates based on Murrell and Pozio (2011), who found that 51% of cases were male and the majority of cases was between 20 and 50 years of age, with a median of 33.1. A generalized Beta distribution was fitted to the latter estimates to define the full distribution of cases from age 0 to 90.

In absence of data on the probability of occurrence of the major clinical symptoms of acute trichinellosis, we assumed, as a worst case scenario, that all patients would develop diarrhoea, facial oedema, myalgia and fever/headache. Because no specific DW for trichinellosis is available, DWs were derived for each the outcomes separately. The four clinical symptoms were respectively matched to the GBD2010 health states *Diarrhoea: moderate* (DW=0.202), *Disfigurement: level 2, with itch or pain* (DW=0.187), *Musculoskeletal problems: generalised, moderate* (DW=0.292), and *Infectious disease: acute episode, severe* (DW=0.210) (Salomon et al., 2012). These four DWs were then aggregated using the multiplicative method, which defines

the aggregated DW as $\sqrt{\sum_{i=1}^n DW_i^2}$. This approach avoids that aggregated DWs would become larger than one and thus "worse than death" (Haagsma et al., 2011).

Based on the systematic review, disease duration ranged from 21.5 to 70 days (Murrell and Pozio, 2011). These values were divided by 365 to express the duration in years.

Given the controversy regarding the existence and nature of chronic trichinellosis, we performed a scenario analysis to assess how the global burden of trichinellosis would change if chronic trichinellosis would indeed exist. Based on a case series of chronic trichinellosis patients from Romania (Nemet et al., 2009), we assumed that 10 to 40% of acute trichinellosis patients would developed chronic sequelae, which would last for a maximum of two years. We further assumed that such patients would suffer from myalgia and fatigue. Again, proxy DWs were derived from Salomon et al. (2012), i.e., *Musculoskeletal problems: generalised, moderate* (DW=0.292) and *Infectious disease: post-acute consequences* (DW=0.254), respectively. These were then combined using the multiplicative approach, yielding an aggregated DW of 0.472.

All DALY calculations were performed in a probabilistic framework, using 10,000 Monte Carlo simulations to compute DALY credible intervals (CrI) based on the uncertainty in the various input parameters. The calculations were performed in R 3.0.1 (R Core Team, 2013), based on the functions available in the DALY package version 1.2.0 (Devleesschauwer et al., 2013a). DALYs were calculated as rates per billion people and, for comparison purposes, as absolute values by applying the DALY rates to the 2010 population (available from

<http://www.census.gov/ipc/www/idb/worldpop.php>). No age weighting or time discounting was applied.

3. Results

Table 1 summarizes the global and regional *Trichinella* burden estimates. Between 1986 and 2009, an average of 2739 cases and 2 deaths were reported per year (Murrell and Pozio, 2011). When applying our correction factors, upper limits were obtained of 5751 cases and 5 deaths per year. These estimates led to a global incidence rate of 469.2 to 985.3 cases per billion per year, and a global mortality rate of 0.300 to 0.828 per billion per year. The estimated global number of DALYs per billion per year was 76 (95% CrI: 38–129; Figure 1). When applied to the 2010 population, this led to a number of 523 DALYs (95% CrI: 263–882). The WHO European region was responsible for 69% (95% CrI: 61%–77%) of this global burden. The scenario analysis further showed that including chronic trichinellosis could increase the global burden by 53% (95% CrI: 26%–84%), to an estimated number of 1108 DALYs (95% CrI: 405–2386).

[TABLE 1]

[FIGURE 1]

4. Discussion

This study provides the first estimate of the global burden of trichinellosis expressed in DALYs. Given the limited data and knowledge on some key clinical aspects of human trichinellosis, the

presented estimates have some limitations. First, due to a lack of knowledge on the occurrence of the different possible clinical outcomes of trichinellosis, we assumed that all cases present with diarrhoea, facial oedema, myalgia and fever/headache. This represents a worst case scenario, and may thus overestimate the global burden of trichinellosis. Second, as no DWs are available for facial oedema or myalgia, we had to apply DWs for "proxy" health outcomes. Third, because the existence of a chronic form of trichinellosis is still questioned, we did not include it in our base estimates. Our scenario analysis showed however that chronic trichinellosis, if it were to exist, could greatly increase the global burden of trichinellosis. This highlights the need for more long-term follow-up studies, studying the extent and nature of chronic trichinellosis, and its correlation with the severity during the acute stage and the time between infection and treatment. Finally, given the lack of information on the level of underreporting of clinical trichinellosis in most parts of the world, we had to resort to arbitrary correction factors to derive plausible upper bounds of the "true" incidence and mortality rates. Further studies are needed to generate evidence-based correction factors.

Notwithstanding these limitations, even when considering the upper bounds of the DALY credible intervals, the global burden of trichinellosis appears very low compared to other foodborne parasitic diseases. Indeed, foodborne trematodosis, alveolar echinococcosis and congenital toxoplasmosis are each responsible for several hundreds of thousands of DALYs worldwide (Furst et al., 2012; Torgerson et al., 2010; Torgerson and Mastroiacovo, 2013). Moreover, the global burden of trichinellosis appears lower than the burden of neurocysticercosis and congenital toxoplasmosis in Nepal alone (Devleesschauwer et al., 2014).

211 The low burden of trichinellosis also contrasts with the high yearly budget allocated to prevent
212 the disease at farm and slaughterhouse level in many industrialized countries (Kapel, 2005;
213 Murrell and Pozio, 2000). The question arises whether the low burden of trichinellosis results
214 from these strong prevention measures or whether the latter are obsolete in industrialized
215 countries where pigs are intensively reared. Both statements are probably true. *Trichinella* meat
216 inspection probably prevented many cases of human infections decades ago when small pig farms
217 with outdoor access were more common. The controlled housing of pig farming systems literally
218 eliminated any possible route of infection, avoiding any contact between pigs and the infected
219 environment, i.e., infected meat from wild or other domestic animals (Thompson, 2013). Within
220 the EU, however, both controlled and non-controlled pig farming systems are still present, the
221 latter especially in central and eastern Europe. Moreover, organic pig farming allowing free-
222 ranging of the animals is an emerging trend in western European countries and in the US (15).
223 Therefore, the EU and the US Department of Agriculture (USDA) are currently considering new
224 regulations that would exempt *Trichinella*-free certified pig farms from meat inspection
225 (SANCO/2378/2006 amending EC No 2075/2005; (Pyburn et al., 2005)). Certified farms would
226 be subjected to a strict regulation and should fulfil specific criteria including physical barriers
227 which prevent contact with other animals, animal carcasses, or exposure to meat-containing
228 waste (Kapel, 2005; Murrell, 2013). In addition to these new measures, the EU permits
229 exemption from meat inspection to regions or countries that obtained negligible risk status based
230 on risk-based surveillance as it is the case for Denmark and Belgium (EC, No 2075/2005). These
231 evolutions towards risk-based control strategies for *Trichinella* are further supported by the
232 observation that an increasing number of the human trichinellosis cases, and thus of trichinellosis
233 DALYs, can be attributed to other animals than domestic pigs (Murrell and Pozio, 2011).

234

5. Conclusion

Globally, trichinellosis is responsible for a minimal human health burden, strengthening the need for replacing current *Trichinella* meat inspection regulations by more cost-effective protocols. To provide a full picture of the disease burden and to decrease the uncertainty around the available estimates, there is a need for studies on the level of underreporting of clinical trichinellosis and for prospective epidemiological and clinical studies, considering both acute and chronic syndromes.

Acknowledgements

This work was commissioned by the Foodborne Disease Burden Epidemiology Reference Group (FERG) of the World Health Organization, and conducted as an in-kind contribution. BD, NP, NS, PT and JAH are FERG members. **References**

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336 **Tables**

337

338 Table 1: Trichinellosis incidence rates, mortality rates, DALY rates and 2010 DALYs

WHO region ^a	Incidence rate per 1e9 (raw; adjusted ^b)	Mortality rate per 1e9 (raw; adjusted ^b)	DALY rate per 1e9 (95% CrI) ^c	2010 DALYs (95% CrI) ^c
AFRO	1.9; 11.4	0.068; 0.408	12 (4–20)	10 (3–17)
AMRO	377.7; 755.4	0.526; 1.052	82 (48–128)	76 (44–119)
EMRO	4.4; 26.4	0.000; 0.000	1 (0–3)	1 (0–2)
EURO	2728.8; 5457.6	1.151; 2.301	405 (202–681)	363 (181–610)
SEARO	6.3; 37.6	0.029; 0.172	6 (2–11)	12 (4–21)
WPRO	34.3; 205.6	0.153; 0.918	34 (12–61)	62 (21–110)
Global	469.2; 985.3	0.300; 0.828	76 (38–129)	523 (263–882)

339 ^a AFRO: WHO African Region; AMRO: WHO Region of the Americas; EMRO: WHO Eastern Mediterranean Region; EURO: WHO
 340 European Region; SEARO: WHO South-East Asia Region; WPRO: WHO Western Pacific Region.

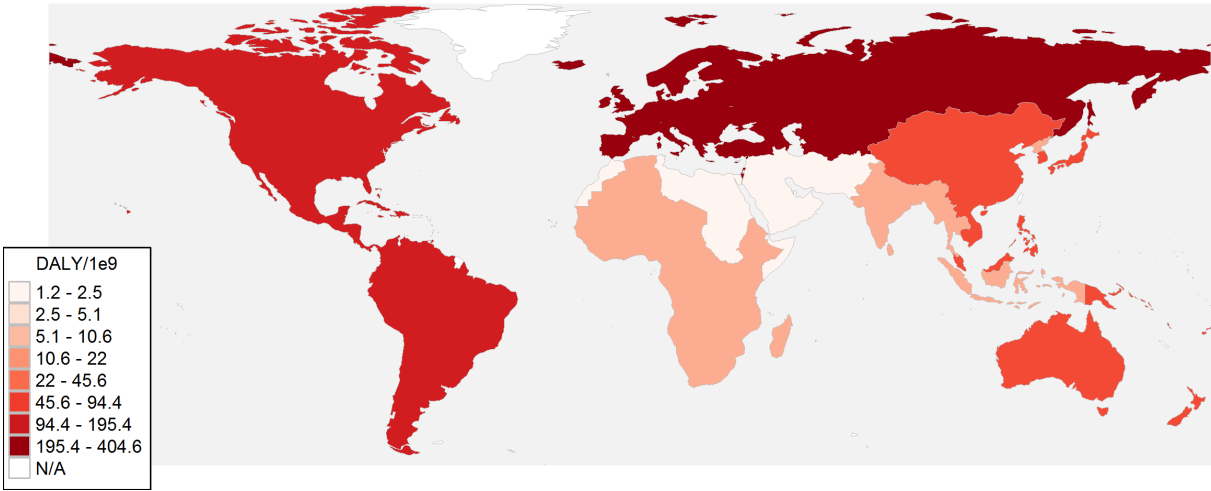
341 ^b To adjust for underreporting, an correction factor of 6 was assumed for AFRO, EMRO, SEARO and WPRO, and an correction factor
 342 of 2 for AMRO and EURO.

343 ^c CrI = Credible Interval.

344 **Figure captions**

345

346 Figure 1. Global burden of trichinellosis by WHO region



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